Request — Jan Deleuran

137653

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabiha Qazi Examiner #: 74194 Date: 11/12/02
Art Unit: 1616 Phone Number: 20622 Serial Number: 10/613,714
Mail Box and Bldg/Room Location: 4C70, Rm, 4A45 Results Format Preferred (circle): PAPER DISK E-MAIL
If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Therapeutic amides

Inventor(s) (please provide full names): Corbett et al

Earliest Priority Filing Date: 7/31/2002

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for compds of Cl, I & 12 when A = C.

Please note Z can be heterocyclic or amino acid, probably Z can be searched as N or Heterocyclic

Please see attached sheet

Thank you

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: [illegible]	NA Sequence (#)	STN ✓
Searcher Phone #: 22504	AA Sequence (#)	Dialog
Searcher Location:	Structure (#) ✓	Questel/Orbit
Date Searcher Picked Up: 11/14	Bibliographic	Dr Link
Date Completed: 11/14	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 10	Patent Family	WWW/Internet
Online Time: 125	Other	Other (specify)

PTO-1590 (8-01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 13:46:42 ON 14 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   12 NOV 2004  HIGHEST RN 780001-49-2
DICTIONARY FILE UPDATES:  12 NOV 2004  HIGHEST RN 780001-49-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l16
L3                STR
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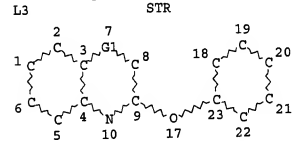

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE
L4  (      2621)SEA FILE=REGISTRY SSS FUL L3
L5                STR
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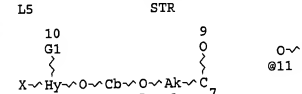

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GGCAT   IS MCY  AT   4
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 N  AT   2
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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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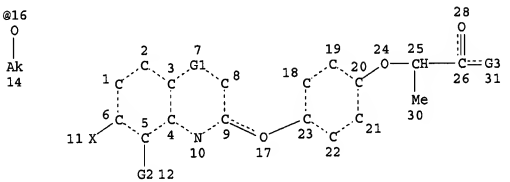
L14 STR



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VAR G3=N/HY
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DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE
L16 29 SEA FILE=REGISTRY SUB=L6 SSS FUL L14

100.0% PROCESSED 663 ITERATIONS 29 ANSWERS
SEARCH TIME: 00.00.01

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L16 29 S L14 FUL SUB=L6
SAV L16 QAZI613C/A

FILE 'HCAPLUS' ENTERED AT 13:42:01 ON 14 NOV 2004
L17 5 S L16
L18 4 S L17 AND (HORWITZ J? OR CORBETT T? OR PALOMINO E? OR POLIN L?
L19 1 S L17 NOT L18
SEL RN L18

FILE 'REGISTRY' ENTERED AT 13:43:37 ON 14 NOV 2004
L20 189 S E1-E189
L21 59 S L20 AND L2 NOT L16
L22 2 S L21 AND C17H14CLN3O3
L23 1 S L22 NOT ALANINE
L24 30 S L16,L23
SAV L24 QAZI613D/A

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L25 0 S L24

FILE 'HCAPLUS' ENTERED AT 13:46:17 ON 14 NOV 2004

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L26             5 S L24

     FILE 'USPATFULL' ENTERED AT 13:46:21 ON 14 NOV 2004
L27             2 S L24

     FILE 'HCAPLUS' ENTERED AT 13:46:35 ON 14 NOV 2004
L28             5 S L26 AND L18-L19

     FILE 'REGISTRY' ENTERED AT 13:46:42 ON 14 NOV 2004

=> fil uspatfull
FILE 'USPATFULL' ENTERED AT 13:46:55 ON 14 NOV 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 11 Nov 2004 (20041111/PD)
FILE LAST UPDATED: 11 Nov 2004 (20041111/ED)
HIGHEST GRANTED PATENT NUMBER: US6817028
HIGHEST APPLICATION PUBLICATION NUMBER: US2004226068
CA INDEXING IS CURRENT THROUGH 11 Nov 2004 (20041111/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 11 Nov 2004 (20041111/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

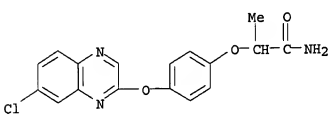
=> d l27 bib abs hitstr tot

L27  ANSWER 1 OF 2  USPATFULL on STN
AN     2004:172454  USPATFULL
TI     Therapeutic amides
IN     Horwitz, Jerome P., Farmington Hills, MI, UNITED STATES
       Corbett, Thomas H., Grosse Pointe Park, MI, UNITED STATES
       Palomino, Eduardo, Royal Oak, MI, UNITED STATES
       Polin, Lisa, Oak Park, MI, UNITED STATES
       Hazeldine, Stuart T., Taylor, MI, UNITED STATES
PI     US 2004132618      A1   20040708
AI     US 2003-613914     A1   20030703 (10)
PRAI   US 2002-393858P     20020703 (60)
DT     Utility
FS     APPLICATION
LREP   Schwegman, Lundberg, Woessner & Kluth, P.A., P.O. Box 2938, Minneapolis,
       MN, 55402
```

CLMN Number of Claims: 64
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2012
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides compounds of the formula: ##STR1##

wherein A, X, Y, and Z are as defined in the specification. The compounds are effective anti-tumor agents. The invention also provides pharmaceutical compositions comprising a compound of the above formula or a salt thereof, intermediates useful for preparing a compound of the above formula, and therapeutic methods comprising administering a compound of the above formula or a salt thereof to a mammal in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **347162-71-4P 347162-73-6P 643752-97-0P**
643752-98-1P 643753-00-8P 643753-02-0P
643753-03-1P 643753-05-3P 643753-06-4P
643753-11-1P 643753-12-2P 643753-13-3P
(preparation of therapeutic amides as antitumor agents)
RN 347162-71-4 USPATFULL
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]- (9CI) (CA INDEX NAME)



RN 347162-73-6 USPATFULL
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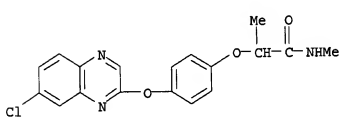
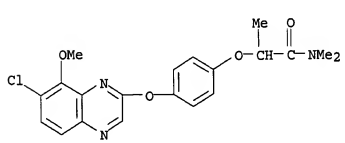
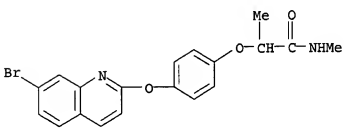


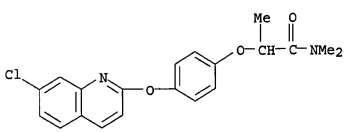
RN 643752-97-0 USPATFULL
CN Propanamide, 2-[4-[(7-chloro-8-methoxy-2-quinoxalinyl)oxy]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



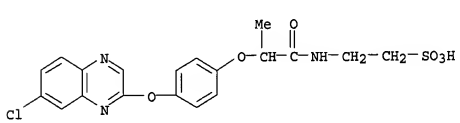
RN 643752-98-1 USPATFULL
CN Propanamide, 2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



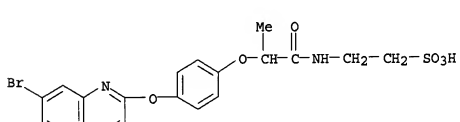
RN 643753-00-8 USPATFULL
CN Propanamide, 2-[4-[(7-chloro-2-quinolinyl)oxy]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



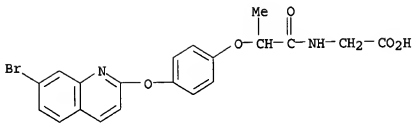
RN 643753-02-0 USPATFULL
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



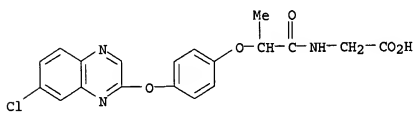
RN 643753-03-1 USPATFULL
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



RN 643753-05-3 USPATFULL
CN Glycine, N-[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

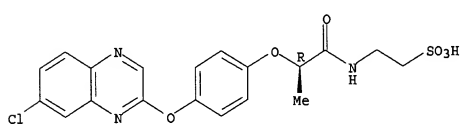


RN 643753-06-4 USPATFULL
CN Glycine, N-[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

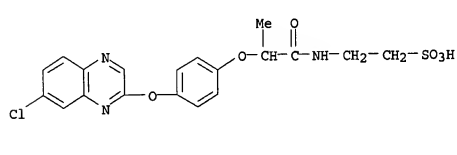


RN 643753-11-1 USPATFULL
CN Ethanesulfonic acid, 2-[[(2R)-2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

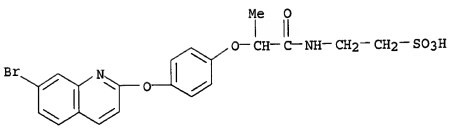


RN 643753-12-2 USPATFULL
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

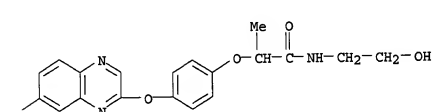
RN 643753-13-3 USPATFULL
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



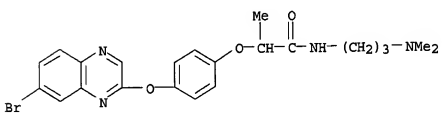
● Na

L27 ANSWER 2 OF 2 USPATFULL on STN
AN 97:115278 USPATFULL
TI (2-quinoxalinyloxy) phenoxypropanoic acids and related derivatives as anticancer agents
IN Behrens, Carl Henry, Newark, DE, United States
Dusak, Betsy Ann, Secane, PA, United States
Harrison, Barbara Ann, Wilmington, DE, United States
Orwat, Michael James, Wilmington, DE, United States
PA The DuPont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)
PI US 5696119 19971209
AI US 1994-367481 19941228 (8)
RLI Continuation of Ser. No. US 1992-991525, filed on 15 Dec 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Bernhardt, Emily
LREP Ferguson, Blair Q., Vance, David H.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1199
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to (2-quinoxalinyloxy)phenoxypropanoic acids, related derivatives thereof, enantiomeric and diastereomeric forms thereof, mixtures of enantiomeric diastereomeric forms thereof, and pharmaceutically acceptable salt forms thereof, pharmaceutical compositions containing them, processes for their preparation, and methods of using them to treat cancer, particularly solid tumors, in mammals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **157435-00-2P 157435-01-3P**
(preparation of, as neoplasm inhibitor)
RN 157435-00-2 USPATFULL
CN Propanamide, 2-[4-[(7-bromo-2-quinoxalinyl)oxy]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 157435-01-3 USPATFULL
CN Propanamide, 2-[4-[(7-bromo-2-quinoxalinyl)oxy]phenoxy]-N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



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FILE COVERS 1907 - 14 Nov 2004 VOL 141 ISS 21
FILE LAST UPDATED: 12 Nov 2004 (20041112/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l28 all hitstr tot

L28 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41446 HCAPLUS
DN 140:111288
ED Entered STN: 18 Jan 2004
TI Preparation of 2-[4-[(7-halo-2-quinolinyl)oxy]phenoxy]propionic acid derivatives and quinoxalinyl analogs as antineoplastic agents
IN **Horwitz, Jerome P.; Corbett, Thomas H.; Palomino, Eduardo; Polin, Lisa; Hazeldine, Stuart T.**
PA Wayne State University, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D215-22
ICS C07D241-44; A61K031-47; A61K031-498; A61P035-00
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004005260 A1 20040115 WO 2003-US21062 20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004132618 A1 20040708 US 2003-613914 20030703
PRAI US 2002-393858P P 20020703
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004005260	ICM	C07D215-22
	ICS	C07D241-44; A61K031-47; A61K031-498; A61P035-00

OS MARPAT 140:111288
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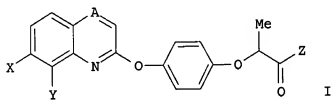

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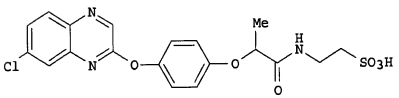


II

AB Title compds. I [wherein A = CH or N; X = F, Cl, or Br; Y = H, OH, or alkoxy; Z = an amino acid or heterocycle; and pharmaceutically acceptable salts thereof] were prepared and tested in vivo as antitumor agents. Preferred compds. of the invention and their pharmaceutical compns. are more potent and less toxic than the known antitumor agent, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]propanoic acid sodium salt (XK 469), and have a different metabolic profile than XK 469. For example, XK 469 was refluxed with SOCl2 for 1 h and the resulting acid chloride treated with β-aminoethylsulfonate (taurine) and 1M NaOH in THF to give II•Na (74%). Chiral HPLC separation afforded the enantiomers. (R)-II•Na was well tolerated in mice at a total dose of 1610 mg/kg i.v. and was highly active (T/C = 0%, log cell kill = 4.2) against early stage murine mammary adenocarcinoma 16/C. No adverse symptoms or cures were noted post injection.

ST quinolinyloxyphenoxy quinoxalinyloxyphenoxy propanoic acid prepn antitumor agent

IT Drug delivery systems
(aerosols; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT Drug delivery systems
(capsules; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid

derivs. and quinoxalinyl analogs as antineoplastic agents)

IT Drug delivery systems
(injections; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT Drug delivery systems
(oral; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT Antitumor agents
Human
Neoplasm
(preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT Drug delivery systems
(tablets; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT **643753-12-2P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT **646505-47-7P 647026-59-3P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

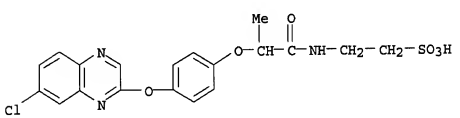
IT 445041-69-0P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT **347162-71-4P 347162-73-6P** 445041-75-8P, (R)-2-[4-[(7-Bromo-2-quinolinyl)oxy]phenoxy]propionic acid **643752-97-0P 643753-00-8P**, 2-[4-[(7-Chloro-2-quinolinyl)oxy]phenoxy]-N,N-dimethylpropionamide **643753-13-3P 646505-48-8P 646505-49-9P**, (R)-[[2-[4-[(7-Bromoquinolin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **646505-50-2P**, (R)-[[2-[4-[(7-Chloroquinoxalin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid 646505-51-3P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT 445041-74-7P, (R)-2-[4-[(7-Chloro-2-quinolinyl)oxy]phenoxy]propionic acid **643752-98-1P**, 2-[4-[(7-Bromo-2-quinolinyl)oxy]phenoxy]-N-methylpropionamide **643753-02-0P 643753-03-1P 643753-05-3P**, [[2-[4-[(7-Bromoquinolin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **643753-06-4P**, [[2-[4-[(7-Chloroquinoxalin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **647026-61-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

IT 56-40-6, Glycine, reactions 613-77-4, 2,7-Dichloroquinoline 7347-25-3 94050-90-5, (R)-(+)-2-(4-Hydroxyphenoxy)propionic acid 99455-15-9,

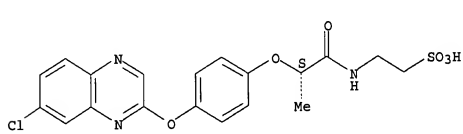
7-Bromo-2-chloroquinoline 157434-99-6, XK 469 157542-89-7
157542-90-0 445041-70-3, 2-[4-[(7-Bromo-2-quinolinyl)oxy]phenoxy]propion
ic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and
quinoxalinyl analogs as antineoplastic agents)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Corbett, T; INVESTIGATIONAL NEW DRUGS 1998, V16(2), P129 HCAPLUS
(2) Ikai, T; US 4629493 A 1986 HCAPLUS
(3) Stuart, H; J MED CHEM 2001, V44, P1758
(4) Zi, K; US 6197728 B1 2001 HCAPLUS
IT **643753-12-2P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
activity); PEP (Physical, engineering or chemical process); PYP (Physical
process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic
acid derivs. and quinoxalinyl analogs as antineoplastic agents)
RN 643753-12-2 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-
oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

IT **646505-47-7P 647026-59-3P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
activity); PUR (Purification or recovery); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic
acid derivs. and quinoxalinyl analogs as antineoplastic agents)
RN 646505-47-7 HCAPLUS
CN Ethanesulfonic acid, 2-[[(2S)-2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-
1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)

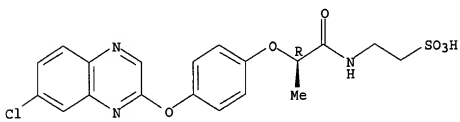
Absolute stereochemistry.



● Na

RN 647026-59-3 HCAPLUS
CN Ethanesulfonic acid, 2-[[(2R)-2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)

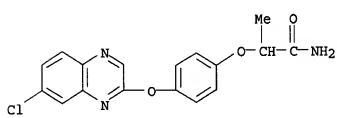
Absolute stereochemistry. Rotation (+).



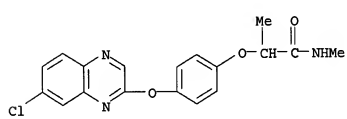
● Na

IT **347162-71-4P 347162-73-6P 643752-97-0P**
643753-00-8P, 2-[4-[(7-Chloro-2-quinolinyl)oxy]phenoxy]-N,N-dimethylpropionamide **643753-13-3P 646505-48-8P**
646505-49-9P, (R)-[[2-[4-[(7-Bromoquinolin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **646505-50-2P**,
(R)-[[2-[4-[(7-Chloroquinoxalin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

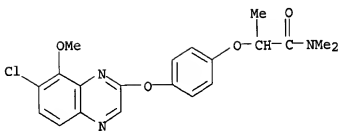
RN 347162-71-4 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]- (9CI) (CA INDEX NAME)



RN 347162-73-6 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 643752-97-0 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-8-methoxy-2-quinoxalinyl)oxy]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



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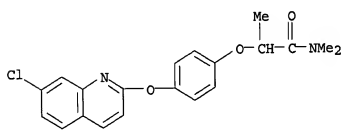
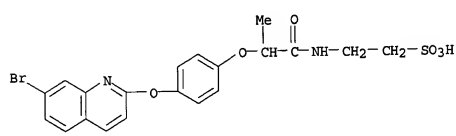
CN Propanamide, 2-[4-[(7-chloro-2-quinolinyl)oxy]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



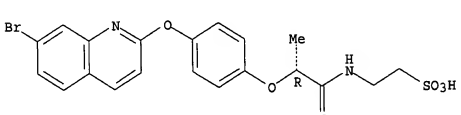
RN 643753-13-3 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 646505-48-8 HCAPLUS
CN Ethanesulfonic acid, 2-[[(2R)-2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● Na

RN 646505-49-9 HCAPLUS
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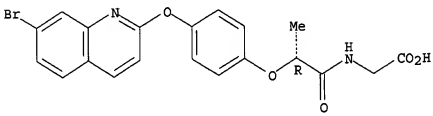
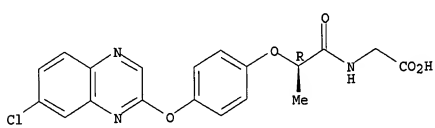
Absolute stereochemistry. Rotation (+).



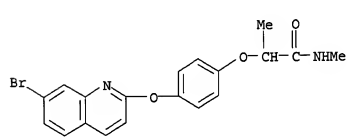
RN 646505-50-2 HCAPLUS
CN Glycine, N-[(2R)-2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

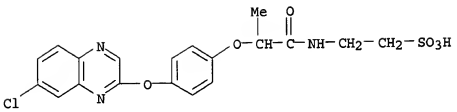


IT **643752-98-1P**, 2-[4-[(7-Bromo-2-quinolinyl)oxy]phenoxy]-N-methylpropionamide **643753-02-0P** **643753-03-1P** **643753-05-3P**, [[2-[4-[(7-Bromoquinolin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **643753-06-4P**, [[2-[4-[(7-Chloroquinoxalin-2-yl)oxy]phenoxy]propionyl]amino]acetic acid **647026-61-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of [[(haloquinolinyl)oxy]phenoxy]propionic acid derivs. and quinoxalinyl analogs as antineoplastic agents)

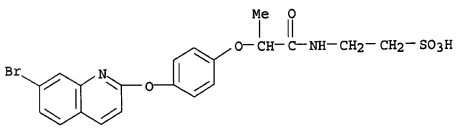
RN 643752-98-1 HCAPLUS
CN Propanamide, 2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



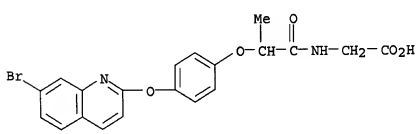
RN 643753-02-0 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



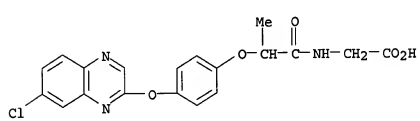
RN 643753-03-1 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



RN 643753-05-3 HCAPLUS
CN Glycine, N-[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

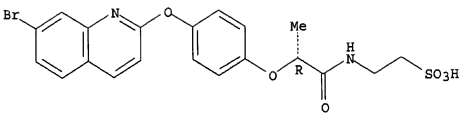


RN 643753-06-4 HCAPLUS
CN Glycine, N-[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)



RN 647026-61-7 HCAPLUS
CN Ethanesulfonic acid, 2-[[(2R)-2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L28 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41220 HCAPLUS
DN 140:99632
ED Entered STN: 18 Jan 2004
TI Preparation of therapeutic amides as antitumor agents
IN **Horwitz, Jerome P.; Corbett, Thomas H.; Palomino, Eduardo; Polin, Lisa; Hazeldine, Stuart T.**
PA Wayne State University, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 28

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004004651	A2	20040115	WO 2003-US21126	20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004132618	A1	20040708	US 2003-613914	20030703
PRAI US 2002-393858P	P	20020703		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004004651	ICM	A61K

OS MARPAT 140:99632

AB Amides, e.g., 2-{4-((7-bromo-2-quinolinyl)oxy)phenoxy}propionmethylamide, {2-{4-(7-bromoquinolin-2-yloxy)phenoxy}propionylamino}acetic acid, or 4-(7-chloro-2-quinolinyl)oxyphenoxypropionylaminoethanesulfonic acid,are prepared for use as effective antitumor agents. The invention also provides pharmaceutical compns. comprising the above compound, intermediates useful for preparing the compds., and methods for administering the compds. to a mammal. Thus, sodium (2-(4-(7-chloro-2-quinolinyl)oxy)phenoxy)propionylam inoethanesulfonate was prepared in a series of steps by starting from Et vinyl ether with oxalyl chloride followed by treatment with substituted anilines cyclization, and subsequent treatment with 2-(4-hydroxyphenoxy)propionic acid. Tablets contained the above compound 100.0, lactose 77.5, Povidone 15.0, Croscarmellose sodium 12.0, microcryst. cellulose 92.5, and Mg stearate 3.0 mg/tablet. The compound had activity against adenocarcinoma.

ST therapeutic amide antitumor prepn
IT Carcinoma

(adenocarcinoma; preparation of therapeutic amides as antitumor agents)
IT Drug delivery systems
(aerosols; preparation of therapeutic amides as antitumor agents)
IT Drug delivery systems
(capsules; preparation of therapeutic amides as antitumor agents)
IT Drug delivery systems
(injections; preparation of therapeutic amides as antitumor agents)
IT Antitumor agents
Neoplasm
(preparation of therapeutic amides as antitumor agents)
IT Amides, biological studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of therapeutic amides as antitumor agents)
IT Drug delivery systems
(tablets; preparation of therapeutic amides as antitumor agents)
IT 23952-31-0P 59412-12-3P 99455-13-7P 160893-07-2P 455955-27-8P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of therapeutic amides as antitumor agents)
IT **347162-71-4P 347162-73-6P 643752-97-0P**
643752-98-1P 643753-00-8P 643753-02-0P
643753-03-1P 643753-05-3P 643753-06-4P
643753-11-1P 643753-12-2P 643753-13-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of therapeutic amides as antitumor agents)
IT 56-40-6, Glycine, reactions 79-37-8, Oxalyl chloride 107-35-7, Taurine 108-42-9 108-44-1, reactions 109-92-2, Ethyl vinyl ether 372-19-0 536-90-3 591-19-5 67648-61-7 94050-90-5 99471-66-6, trans-3-Ethoxyacryloyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of therapeutic amides as antitumor agents)
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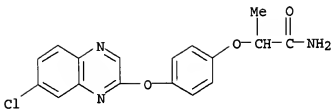
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of therapeutic amides as antitumor agents)
IT **347162-71-4P 347162-73-6P 643752-97-0P**
643752-98-1P 643753-00-8P 643753-02-0P
643753-03-1P 643753-05-3P 643753-06-4P
643753-11-1P 643753-12-2P 643753-13-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of therapeutic amides as antitumor agents)
RN 347162-71-4 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]- (9CI) (CA INDEX NAME)



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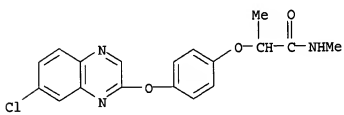

RN 643752-97-0 HCAPLUS
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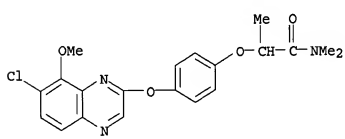

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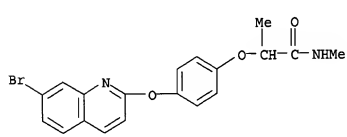

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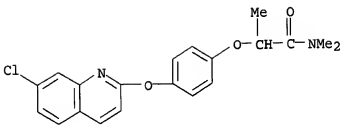
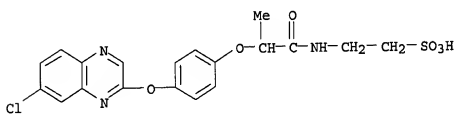
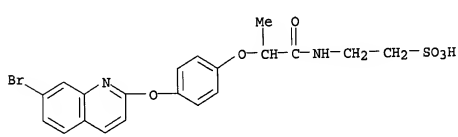


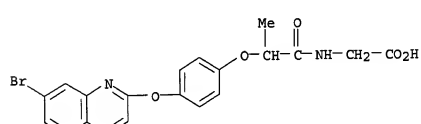
RN 643753-02-0 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



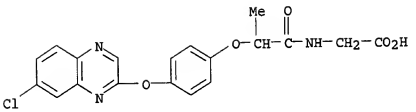
RN 643753-03-1 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



RN 643753-05-3 HCAPLUS
CN Glycine, N-[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

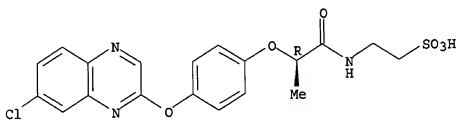


RN 643753-06-4 HCAPLUS
CN Glycine, N-[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]- (9CI) (CA INDEX NAME)

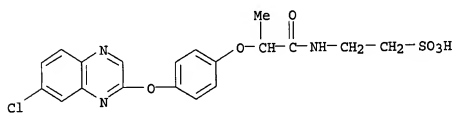


RN 643753-11-1 HCAPLUS
CN Ethanesulfonic acid, 2-[[(2R)-2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

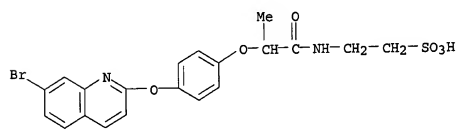


RN 643753-12-2 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



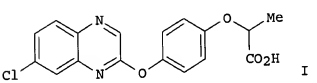
● Na

RN 643753-13-3 HCAPLUS
CN Ethanesulfonic acid, 2-[[2-[4-[(7-bromo-2-quinolinyl)oxy]phenoxy]-1-oxopropyl]amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L28 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:301100 HCAPLUS
DN 135:76849
ED Entered STN: 29 Apr 2001
TI Design, Synthesis, and Biological Evaluation of Analogues of the Antitumor Agent, 2-{4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy}propionic Acid (XK469)
AU **Hazeldine, Stuart T.**; **Polin, Lisa**; Kushner, Juiwanna; Paluch, Jennifer; White, Kathryn; Edelstein, Matthew; **Palomino, Eduardo**; **Corbett, Thomas H.**; **Horwitz, Jerome P.**
CS Department of Internal Medicine Division of Hematology and Oncology, Wayne State University School of Medicine, Detroit, MI, 48201, USA
SO Journal of Medicinal Chemistry (2001), 44(11), 1758-1776
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 28-18 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
OS CASREACT 135:76849
GI



I

AB 2-{4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy}propionic acid (XK469) I is among the most highly and broadly active antitumor agents to have been evaluated and scheduled to enter clin. trials in 2001. The mechanism or mechanisms of action of I remain to be elaborated. Accordingly, an effort was initiated to establish a pharmacophore hypothesis to delineate the requirements of the active site, via a comprehensive program of synthesis of analogs of I and evaluation of the effects of structural modification(s) on solid tumor activity. The strategy formulated chose to dissect the two-dimensional parent structure into three regions: I, ring A of quinoxaline; II, the hydroquinone connector linkage; and III, the lactic acid moiety-to determine the resultant in vitro and in vivo effects of chemical alterations in each region. Neither the A-ring unsubstituted nor the B-ring 3-chloro-regioisomer of I showed antitumor activity. The modulating antitumor effect(s) of substituents of differing electronegativities, located at the several sites comprising the A-ring of region I, were next ascertained. Thus, a halogen substituent, located at the 7-position of a 2-{4-[(2-quinoxalinyl)oxy]phenoxy}propionic acid, generated the most highly and broadly active antitumor agents. A Me, methoxy, or an azido substituent at this site generated a much less active structure, whereas 5-, 6-, 8-chloro-, 6-, 7-nitro, and 7-amino derivs. all proved to be essentially inactive. When the connector linkage (region II) of I was changed from that of a hydroquinone to either a resorcinol or a catechol derivative, all antitumor activity was lost. Of the carboxylic acid derivs. of I (region III), i.e., CONH2, CONHMe, CONMe2, CONHOH, CONHNH2, CN, or CN4H (tetrazole), only the monomethyl- and N,N-dimethylamides proved to be active.

ST chloroquinoxalinyloxyphenoxypropionic acid structure antitumor; quinoxalinyloxyphenoxypropionic acid antitumor prepn

IT Structure-activity relationship
(antitumor; preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs from (chloro)quinoxalonols)

IT Antitumor agents
(preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs from (chloro)quinoxalonols)

IT 347162-49-6P
RL: BYP (Byproduct); PREP (Preparation)
(formation of (oxoquinoxalinyl)propionate byproduct in preparation of antitumor (chloroquinoxalinyloxy)propionic acid from chloroquinoxalinols)

IT 347162-28-1P 347162-30-5P 347162-32-7P 347162-34-9P 347162-36-1P
347162-37-2P 347162-39-4P 347162-41-8P 347162-43-0P 347162-45-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity study of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 106744-85-8P 347162-29-2P 347162-31-6P 347162-33-8P 347162-35-0P
347162-38-3P 347162-40-7P 347162-42-9P 347162-44-1P 347162-46-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity study of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 60075-04-9, Methyl 2-(4-hydroxyphenoxy)propionate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (chloroquinoxalinyloxy)phenoxypropionic acid analogs from chloroquinoxalinols as antitumor agents)

IT 347162-27-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (chloroquinoxalinyloxy)phenoxypropionic acid analogs from chloroquinoxalinols as antitumor agents)

IT 123-30-8, 4-Hydroxyaniline 535-11-5, Ethyl 2-bromopropionate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (phenylamino)propionate in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 35897-44-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (phenylamino)propionate in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 637-89-8, 4-Mercaptophenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (phenylthiopropionate) in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 347162-60-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (phenylthiopropionate) in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT **220935-29-5P** 347162-54-3P 347162-62-3P 347162-64-5P
347162-71-4P 347162-72-5P 347162-73-6P
347162-76-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 21023-20-1 78104-71-9 157435-10-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 347162-53-2P 347162-55-4P 347162-57-6P 347162-61-2P 347162-63-4P
347162-65-6P 347162-66-7P 347162-68-9P 347162-69-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 5445-17-0, Methyl 2-bromopropionate 59489-30-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor (chloroquinoxalinyloxy)propionic acid from chloroquinoxalinols)

IT 347162-48-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor (chloroquinoxalinyloxy)propionic acid from chloroquinoxalinols)

IT 769-11-9, 2-Chloro-6-nitroaniline 59483-54-4, 3-Chloro-2-nitroaniline 89793-13-5 89975-38-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from (chloro)nitroanilines in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 55687-05-3P, 2,5-Dichloroquinoxaline 55687-19-9P 65180-12-3P
120258-69-7P 347162-12-3P 347162-13-4P 347162-14-5P 347162-19-0P
347162-20-3P 347162-21-4P 347162-22-5P 347162-23-6P 347162-24-7P
347162-25-8P 347162-26-9P 347162-92-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from (chloro)nitroanilines in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 20691-72-9, 4-Iodo-2-nitroaniline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from nitroanilines in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 55686-93-6P, 2-Chloro-7-methoxyquinoxaline 59489-31-5P,
2,7-Dichloroquinoxaline 90272-84-7P 347162-15-6P 347162-16-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from nitroanilines in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 25652-34-0 55687-28-0 62573-36-8 66367-04-2 89898-96-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from nitroanilines in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid)

IT 347162-77-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from nitroanilines in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 98555-00-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from quinoxalinols in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 6272-25-9P, 2-Chloro-6-nitroquinoxaline 55686-94-7P,
2-Chloro-7-nitroquinoxaline 347162-17-8P 347162-18-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chloroquinoxalines from quinoxalinols in synthesis of (chloroquinoxalinyloxy)phenoxypropionic acid analogs as antitumor agents)

IT 347162-75-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of inactive antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 347162-47-4P 347162-56-5P 347162-58-7P 347162-67-8P 347162-70-3P

347162-74-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of inactive antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 347162-50-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of inactive antitumor (chloroquinoxalinyloxy)propionic acid from chloroquinoxalinols)

IT 92-88-6, 4,4'-Dihydroxybiphenyl 108-46-3, 1,3-Dihydroxybenzene, reactions 6272-38-4, 2-(Benzyloxy)phenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of phenoxypropionates in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 87129-34-8P, Methyl 2-(3-hydroxyphenoxy)propionate 138426-35-4P 347162-51-0P 347162-52-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenoxypropionates in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 103-16-2, 4-(Benzyloxy)phenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of phenoxypropionitrile in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

IT 23194-54-9P 343866-65-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenoxypropionitrile in synthesis of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

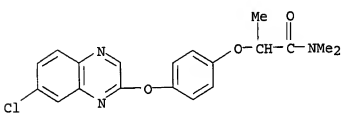
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

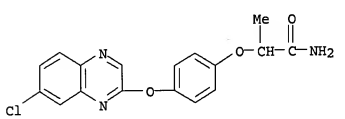
(1) Ahmad, Y; Tetrahedron 1964, V20, P1107 HCAPLUS
(2) Ando, W; Synth Commun 1983, V13, P1053 HCAPLUS
(3) Anon; Personal communication from Professor Lawrence J Marnett, A B Hancock
(4) Atkinson, C; J Chem Soc 1956, P26 HCAPLUS
(5) Biernat, L; Seventh NCI-EORTC symposium on new drugs in cancer therapy Abstract #185 1992
(6) Bischoff, C; Chem Ber 1897, V30, P6
(7) Cheeseman, G; J Chem Soc 1961, P1246 HCAPLUS
(8) Corbett, T; Anticancer drug development guide:Preclinical screening, clinical trials, and approval, Chapter 5 1997, P75 HCAPLUS
(9) Corbett, T; Cancer Res 1984, V44, P717 HCAPLUS
(10) Corbett, T; Cytotoxic anticancer drugs:Models and concepts for drug discovery and development 1992, P33
(11) Corbett, T; Int J Pharmacogn 1995, V33(supp), P102
(12) Corbett, T; Invest New Drugs 1997, V15, P207 HCAPLUS
(13) Corbett, T; Invest New Drugs 1998, V16, P129 HCAPLUS
(14) Dreikhorn, B; US 3979387 1976 HCAPLUS
(15) Gao, H; Proc Natl Acad Sci U S A 1999, V96, P12168 HCAPLUS
(16) Harvey, I; J Chem Soc Perkin Trans 1 1988, P681 HCAPLUS
(17) Kalgutkar, A; J Med Chem 1998, V41, P4800 HCAPLUS
(18) Kessel, D; Cancer Lett 1985, V28, P187 HCAPLUS
(19) Liu, L; DNA topoisomerases in cancer 1991, P13 HCAPLUS
(20) Lorusso, P; Invest New Drugs 1999, V16, P287 MEDLINE
(21) Lorusso, P; Proc Am Assoc Cancer Res 1994, V35, P401
(22) Mallory, F; J Org Chem 1963, V28, P1656 HCAPLUS
(23) Mallory, F; J Org Chem 1964, V29, P2605 HCAPLUS
(24) Platt, B; J Chem Soc 1948, P1310 HCAPLUS
(25) Serban, A; US 4358307 1982 HCAPLUS
(26) Telschow, J; US 4614814 1986 HCAPLUS
(27) Wear, R; J Am Chem Soc 1950, V71, P2893
(28) White, W; J Org Chem 1977, V42, P166 HCAPLUS
(29) Williard, P; Tetahedron Lett 1980, V21, P3731 HCAPLUS
(30) Wolf, F; J Am Chem Soc 1949, V71, P6 HCAPLUS

IT **220935-29-5P 347162-71-4P 347162-72-5P**
347162-73-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)

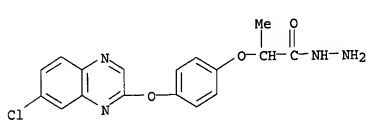
RN 220935-29-5 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



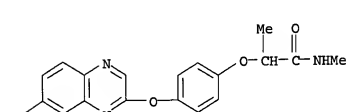
RN 347162-71-4 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]- (9CI) (CA INDEX NAME)



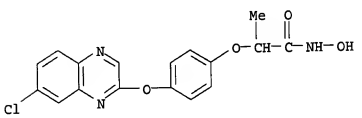
RN 347162-72-5 HCAPLUS
CN Propanoic acid, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-, hydrazide (9CI) (CA INDEX NAME)



RN 347162-73-6 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IT **347162-74-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of inactive antitumor (chloroquinoxalinyloxy)phenoxypropionic acid analogs)
RN 347162-74-7 HCAPLUS
CN Propanamide, 2-[4-[(7-chloro-2-quinoxalinyl)oxy]phenoxy]-N-hydroxy- (9CI) (CA INDEX NAME)



L28 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:787599 HCAPLUS
DN 130:204665
ED Entered STN: 16 Dec 1998
TI Preclinical antitumor efficacy of analogs of XK469: sodium-(2-[4-(7-chloro-2-quinoxalinyloxy)phenoxy]propionate)
AU **Corbett, Thomas H.**; LoRusso, Patricia; Demchick, Lisa; Simpson, Chiab; Pugh, Susan; White, Kathryn; Kushner, Juiwanna; **Polin, Lisa**; Meyer, Jennifer; Czarnecki, Jennifer; Heilbrun, Lance; **Horwitz, Jerome P.**; Gross, Janet L.; Behrens, Carl H.; Harrison, Barbara A.; McRipley, Ron J.; Trainor, George
CS School of Medicine, Wayne State University, Detroit, USA
SO Investigational New Drugs (1998), 16(2), 129-139
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
CC 1-3 (Pharmacology)
AB A series of quinoxaline analogs of the herbicide Assure was found to have selective cytotoxicity for solid tumors of mice in a disk-diffusion-soft-agar-colony-formation-assay compared to L1210 leukemia. Four agents without selective cytotoxicity and 14 agents with selective cytotoxicity were evaluated in vivo for activity against a solid tumor. The four agents without selective cytotoxicity in the disk-assay were inactive in vivo (T/C > 42%). Thirteen of the fourteen agents with selectivity in the disk-assay were active in vivo (T/C < 42%). Five of the agents had curative activity. These five agents had a halogen (F, Cl, Br) in the 7-position (whereas Assure had a Cl in the 6 position). All agents with curative activity were either a carboxylic acid, or a derivative thereof, whereas Assure is the Et ester of the carboxylic acid. All other structural features were identical between Assure and the curative agents. Assure had no selective cytotoxicity for solid tumors in the disk-assay, and was devoid of antitumor activity. The analog XK469 is in clin. development.
ST Assure quinoxaline analog antitumor structure
IT Structure-activity relationship
(antitumor; preclin. antitumor efficacy of quinoxaline analogs of Assure)
IT Antitumor agents
(preclin. antitumor efficacy of quinoxaline analogs of Assure)
IT 76578-13-7 76578-16-0 82073-86-7 110945-24-9 157434-99-6, XK 469 **157435-00-2** 157435-13-7 157542-87-5, XB 947 157542-89-7 157542-90-0 **220935-14-8** **220935-15-9** **220935-16-0** 220935-17-1 **220935-18-2** 220935-20-6

220935-22-8 220935-25-1 220935-27-3
220935-29-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(preclin. antitumor efficacy of quinoxaline analogs of Assure)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

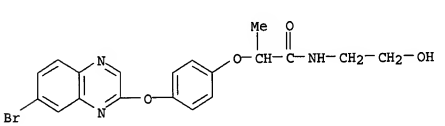
RE

(1) Branda, R; Biochem Pharmacol 1988, V37, P4557 HCAPLUS
(2) Branda, R; Biochem Pharmacol 1989, V38, P3521 HCAPLUS
(3) Conley, B; Cancer Chemother Pharmacol 1995, V37, P139 HCAPLUS
(4) Corbett, T; AACR Abst No 1289 1984, V25, P325
(5) Corbett, T; Cancer 1977, V40(5), P2660 HCAPLUS
(6) Corbett, T; Cancer Res 1975, V35, P2434 HCAPLUS
(7) Corbett, T; Cancer Res 1982, V42, P1707 HCAPLUS
(8) Corbett, T; Cancer Res 1984, V44, P717 HCAPLUS
(9) Corbett, T; Cancer Treat Rep 1982, V66(5), P1187 HCAPLUS
(10) Corbett, T; Cytotoxic Anticancer Drugs:Models and Concepts for Drug Discovery and Development 1992, P33
(11) Corbett, T; Expert Opinion on Investigational Drugs 1994, V3(12), P1281 HCAPLUS
(12) Corbett, T; Intern J Pharmacognosy 1995, V33(Supp), P102
(13) Corbett, T; Invest New Drugs 1987, V5, P3 HCAPLUS
(14) Corbett, T; J Exper Therap Oncol 1996, V1, P95 HCAPLUS
(15) Corbett, T; Rodent Models in Experimental Chemotherapy Chapt 50 1987, P233
(16) Corbett, T; The Anticancer Drug Development Guide:Preclinical Screening, Chapt-5 1997, P75 HCAPLUS
(17) Craciunescu; An R Acad Farm 1985, V51, P653 HCAPLUS
(18) Davis; EP 0323727 A2 HCAPLUS
(19) Fawzi; US 4609396 HCAPLUS
(20) Foster; Invest New Drugs 1985, V3, P401
(21) Katagiri, K; Antibiotics 1974, VIII, P234
(22) Lorusso, P; Preclinical antitumor activity of XK469 EORTC 104 1994
(23) Lorusso, P; Proc of AACR 1994, V35, P401
(24) Miller, V; Cancer Chemother Pharmacol 1997, V40(4), P415
(25) Piatti, S; Anales de Quimica 1989, V85, P105 HCAPLUS
(26) Piatti, S; Anales de Quimica Ser C 1986, V82, P85 HCAPLUS
(27) Rigas, J; Cancer Chemother Pharmacol 1995, V35(6), P483 MEDLINE
(28) Serban; EP 0023785 A2 HCAPLUS
(29) Serban; US 4655819 HCAPLUS
(30) Serban; US 4803273 HCAPLUS
(31) Ura; US 4629493 HCAPLUS
(32) Zegar, I; Chem Biol Interactions 1989, V72, P277 HCAPLUS

IT **157435-00-2 220935-14-8 220935-15-9**
220935-16-0 220935-18-2 220935-22-8
220935-25-1 220935-29-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(preclin. antitumor efficacy of quinoxaline analogs of Assure)

RN 157435-00-2 HCAPLUS

CN Propanamide, 2-[4-[(7-bromo-2-quinoxalinyl)oxy]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 220935-14-8 HCAPLUS

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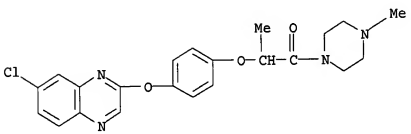

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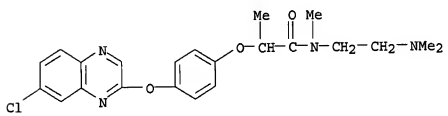

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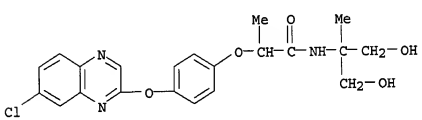

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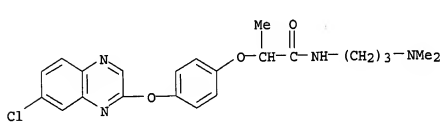

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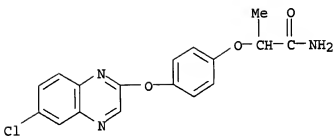

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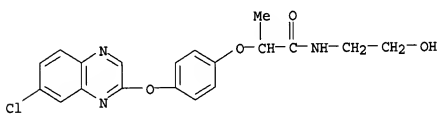

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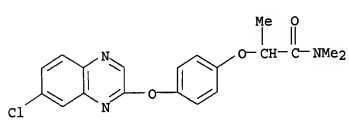


L28 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:557671 HCAPLUS
DN 121:157671
ED Entered STN: 01 Oct 1994
TI 2-[(quinoxalinyloxy)phenoxy]propanoates and related derivatives as anticancer agents
IN Behrens, Carl Henry; Dusak, Betsy Ann; Harrison, Barbara Ann; Orwat, Michael James
PA Du Pont Merck Pharmaceutical Co., USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D241-44
ICS A61K031-495
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9413647	A1	19940623	WO 1993-US11936	19931214

W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

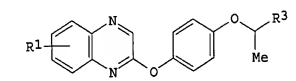
AU 9456867	A1	19940704	AU 1994-56867	19931214
US 5696119	A	19971209	US 1994-367481	19941228
PRAI US 1992-991525		19921215		
WO 1993-US11936		19931214		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9413647	ICM	C07D241-44
	ICS	A61K031-495

OS MARPAT 121:157671

GI



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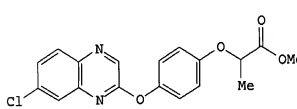


II

AB The title [(2-quinoxalinyloxy)phenoxy]propanoates I (R1 = chloro, bromo; R3 = carboxy, alkoxycarbonyl, amido) were disclosed. The use of I for the treatment of tumors is claimed. Pharmaceutical compns. containing I for the treatment of cancer were described. A prepared example compound is (±)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoic acid [ester of (±)-quizalofop] (II).

ST neoplasm inhibitor quinoxalinyloxyphenoxy propanoate prepn; quizalofop ester prepn neoplasm inhibitor; tumor quinoxalinyloxyphenoxy propanoate prepn; cancer quinoxalinyloxyphenoxy propanoate prepn

IT Neoplasm inhibitors
([(quinoxalinyloxy)phenoxy]propanoates)

IT Neoplasm inhibitors
(leukemia, [(quinoxalinyloxy)phenoxy]propanoates)

IT 78104-71-9P 157435-13-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

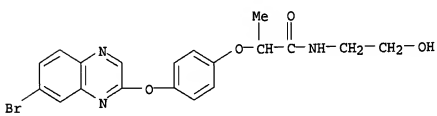
IT 2427-71-6P, 6-Chloro-2-quinoxalinol 18671-97-1P, 2,6-Dichloroquinoxaline 59489-30-4P, 2(1H)-Quinoxalinone, 7-chloro- 59489-31-5P, Quinoxaline, 2,7-dichloro- 157435-07-9P 157435-08-0P 157435-09-1P 157435-11-5P 157435-12-6P 157542-91-1P 157542-92-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for [(quinoxalinyloxy)phenoxy]propanoate neoplasm inhibitor)

IT 76578-13-7P 76578-49-9P 78104-71-9P, Methyl (±)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoate 81466-27-5P 157434-99-6P **157435-00-2P 157435-01-3P** 157435-02-4P 157435-03-5P 157435-05-7P 157435-06-8P 157435-10-4P 157542-87-5P, Methyl (R)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoate 157542-88-6P, Methyl (S)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoate 157542-89-7P, Sodium (R)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoate 157542-90-0P, Sodium (S)-2-[4-[(7-Chloro-2-quinoxalinyl)oxy]phenoxy]propanoate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)

IT 95-83-0, 4-Chloro-1,2-phenylenediamine 103-16-2, p-Benzyloxyphenol 109-55-7, N,N-Dimethyl-1,3-propanediamine 115-69-5, 2-Amino-2-methyl-1,3-propanediol 141-43-5, reactions 298-12-4 17392-83-5, Methyl (R)-lactate 27871-49-4, Methyl (S)-lactate 67648-61-7, Methyl (±)-2-(4-hydroxyphenoxy)propanoate 89891-65-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for [(quinoxalinyloxy)phenoxy]propanoate neoplasm inhibitor)

IT **157435-00-2P 157435-01-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)

RN 157435-00-2 HCAPLUS
CN Propanamide, 2-[4-[(7-bromo-2-quinoxalinyl)oxy]phenoxy]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



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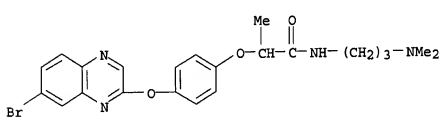

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